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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/897,390	07/21/1997	Matthew Lavail	REG-32	4393

7590 02/24/2003

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EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/897,390	La Vail et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 15, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above, claim(s) *36-38* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-35 and 39-41* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-41* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☒ The oath or declaration is objected to by the Examiner. – no P.O. Box for Steinberg

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 16
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. The amendment filed 7/15/02 has been entered.

2. The rejection of claims 1-5 & 20-25 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,667,968 is withdrawn due to the submission of a terminal disclaimer.

3. The rejections of claims 1-35 under 35 U.S.C. 101, and 112, first paragraph, because the claimed invention is not supported by either a credible asserted utility or a well established utility, is withdrawn due to the amendment of the claims.

4. The rejection of claims 1-35 under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete is withdrawn due to the amendment of the claims.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Applicant's arguments filed 7/15/02 have been fully considered but they are not deemed to be persuasive.

7. This application contains claims 36-38 drawn to an invention nonelected with traverse in Paper No. 6. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

8. Claim 40 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application is apparent for the recitation, "active fragment thereof"; thereby, constituting new matter.

9. Claims 1-35 & 39-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing degeneration of the outer segment of photoreceptor cells following intraocular or systemic administration of the well known neurotrophic factors BDNF, CNTF, NT-3, aFGF, bFGF, IL-1β, TNF-α and IGF-2, does not reasonably provide enablement for any method for "reducing" neurodegeneration of retinal neurons generically with structurally and functionally uncharacterized modified neurotrophic factors/ fragments (i.e., as it especially relates to new claim 40) orally, subcutaneously, intravenously or intramuscularly. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reason made of record in Paper No: 9 (mailed 2/13/02).

Applicants argue on pages 6-8 of the response that "the claims as amended recite administration of a neurotrophic factor effective to reduce retinal degeneration", that "[t]he Office Action acknowledged that eight different factors were effective in reducing degeneration of the outer segment of photoreceptor cells [so] [t]hose skilled in the art would reasonably expect that other neurotrophic factors would also reduce degeneration of retinal neurons", that "[i]f degeneration is reduced to any degree, then use of the neurotrophic factor is encompassed by the claim", and then cites 5 references all with publication dates 12 yrs, 12 yrs, 12 yrs, 11 yrs and 13 yrs after the claimed priority date for the instant application. In that Applicants are correct that they adequately teach eight neurotrophic factors that do show "some degree of rescue of photoreceptors" (and two that do not; i.e., insulin and Il-6), Applicants' arguments are persuasive regarding this particular part of the rejection concerning enabling use of "neurotrophic factors" for "rescue of photoreceptors" (note that "heparin" is not a neurotrophic factor; e.g., see pg. 6 of the specification). However, consistent with the teachings of Rudinger previously made of record, "active fragments thereof" as recited in claim 40 are not enabled for the reasons previously made of record.

Applicants then argue on pages 8-10 of the response that "[i]t follows that oral, subcutaneously, intravenous, and intramuscular administration are also enabled", that "[t]he

specification states that the invention provides methods for reducing degeneration of various retinal cells, including photoreceptors, retinal ganglion cells, displaced retinal ganglion cells, amacrine cells, displaced amacrine cells, and horizontal and bipolar cells", as listed on page 7 (lines 16-21) of the specification, and then cites 4 references all with publication dates 11 yrs, 11 yrs, 12 yrs and 13 yrs after the claimed priority date for the instant application. First, consistent with the teachings of Sendtner and Regeneron's Phase III study on using neurotrophic factors previously made of record, and the well known impermeable nature of the blood-brain-barrier toward proteins in 1989, the route of administration remains enabled for only "intraocular or systemic administration", as previously made of record. Second, because the claims are not limited to "rescue/ reduce degeneration of photoreceptors", Applicants' arguments are not persuasive for any broader scope (i.e., "reducing degeneration of [non-photoreceptor] retinal neurons"); consistent with the teachings of Rapp, the Merck Manual, and Jackowski previously made of record. Enablement must be established in the specification *at the time of filing* and is to be *commensurate in scope* with the stated claims. *In re* Hogan and Banks, 194 USPQ 527 (1977). Further, the courts in *Novo Nordisk v. Genentech*, 42 USPQ2d 1001 (Fed. Cir. (N.Y.), 1997), held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

In other words, an invitation for others to experiment to putatively affect non-photoreceptor cells, which the art in 1989 (i.e., the priority date claimed for the instant invention) did not accept as

being treatable, coupled with the limited guidance provided within the instant specification, in which increased survival of not a single other type of retinal neuron has been disclosed, would not reasonably allow one of ordinary skill in the art at the time the instant invention was filed to know how to make and/or use the invention as currently and broadly claimed, without requiring undue experimentation to determine otherwise. Thus, Applicants' arguments are not persuasive for enabling claims directed toward "reducing degeneration of [non-photoreceptor] retinal neurons", or for other routes of administration, for the reasons made of record.

10. The information disclosure statement filed 7/15/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered for that reference crossed out. Note that no PTP 1449 was submitted for those references listed in the response as Exhibits 1-9.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
February 19, 2003